

### **DETAILED ACTION**

1. Applicants' amendment filed 12 March 2008 is acknowledged, however, as discussed in the notice mailed 9/24/2008, the amendment filed 12 March 2008 does not comply with 37 C.F.R. 1.126. Applicant is reminded that a cancelled claim can be reinstated only by a subsequent amendment presenting the claim as a new claim with a new claim number. Accordingly, the newly added claims (e.g., claims 105-150) filed 5/19/2005 serve as the basis for the instant restriction requirement.

### ***Election/Restrictions***

2. Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

To have a general inventive concept under PCT rule 13.1, the inventions need to be linked by a special technical feature. The special technical feature recited in claim 1 a butyrylcholinesterase variant comprising one of the recited sequences or a functional fragment thereof, wherein the variant or fragment comprises alanine at amino acid position 227. In view of this Sevigny et al (WO 99/66072, 12/23/1999) reads on the claim. Sevigny et al teach the sequence of a human butyrylcholinesterase variant having a single nucleotide polymorphism, which comprises alanine at amino acid position 227 (e.g., Figs. 2 and 4). Therefore the technical feature recited in claim 1 is not special. Accordingly the groups are not so linked as to form a single general concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in response to this action, to elect a single invention to which the claims must be restricted.

Group I, claims 105-117, drawn to a butyrylcholinesterase variant or functional fragment thereof.

Group II, claims 118-119, drawn to a butyrylcholinesterase variant or functional fragment thereof and an antibody that specifically binds EGFR.

Group III, claims 120-121, drawn to a butyrylcholinesterase variant or functional fragment thereof and an antibody that specifically binds CD20.

Group IV, claims 122-123, drawn to a nucleic acid encoding a butyrylcholinesterase variant or fragment thereof.

Group V, claims 124-137, drawn to a method of converting a camptothecin derivative to a topoisomerase inhibitor comprising contacting said camptothecin derivative with a butyrylcholinesterase variant comprising or functional fragment thereof.

Group VI, claims 139-144 and 149-150, drawn to a method of treating cancer comprising administering to an individual an effective amount of a butyrylcholinesterase variant comprising or functional fragment thereof.

Group VII, claims 145-146, drawn to a method of converting a camptothecin derivative to a topoisomerase inhibitor comprising contacting said camptothecin derivative with a butyrylcholinesterase variant comprising or functional fragment thereof and an antibody that specifically binds EGFR.

Group VIII, claims 147-148, drawn to a method of converting a camptothecin derivative to a topoisomerase inhibitor comprising contacting said camptothecin derivative with a butyrylcholinesterase variant comprising or functional fragment thereof and an antibody that specifically binds CD20.

3. In addition, each category of invention detailed above reads on numerous patentably distinct sequences. Each sequence is patentably distinct because they are unrelated sequences, and a further restriction is applied to each Group. For each category of invention set forth above, Applicant(s) must further elect a single sequence

for examination. It is noted that this is a restriction requirement to a single sequence and NOT a species election requirement.

MPEP 803.04 states:

"Nucleotide sequences encoding different proteins are structurally distinct chemical compounds and are unrelated to one another. These sequences are thus deemed to normally constitute independent and distinct inventions with the meaning of 35 U.S.C. 121. Absent evidence to the contrary, each such nucleotide sequence is presumed to represent an independent and distinct invention, subject to a restriction requirement pursuant to 35 U.S.C. 121 and 37 CFR 1.141 et seq."

It has been determined that 1(ONE) sequence constitutes a reasonable number for examination purposes under the present conditions. At present the huge number of submissions of claims directed to various sequences, such as nucleic acids or polypeptides, is so large that the election of 1(one) sequence of this type is now deemed to be practically appropriate so as to not overwhelm the examination and search processes for such claims.

4. Claim 138 links inventions VI, VII and VIII. The restriction requirement among the linked inventions is subject to the nonallowance of the linking claim, claim 138. Upon the indication of allowability of the linking claim, the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise requiring all the limitations of the allowable linking claim will be rejoined and fully examined for patentability in accordance with 37 CFR 1.104. Claims that require all the limitations of an allowable linking claim will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

Applicant(s) are advised that if any claim presented in a continuation or divisional application is anticipated by, or includes all the limitations of, the allowable linking claim, such claim may be subject to provisional statutory and/or nonstatutory double patenting

rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 443 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

5. The inventions listed as Groups I-VIII do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: As set forth above, in view of the teaching of Sevigny et al the groups are not so linked as to form a single general concept under PCT Rule 13.1 because the technical feature of claim 1 is not special.

Inventions of Groups I-IV represent separate and distinct products which are made by materially different methods, and are used in materially different methods which have different modes of operation, different functions and different effects. The butyrylcholinesterase variant of Group I, the butyrylcholinesterase variant and anti-EGFR antibody of Group II, the butyrylcholinesterase variant and the anti-CD20 antibody of Group III and the polynucleotide of Group IV are all structurally and chemically different from each other. The butyrylcholinesterase variant is made by translation of mRNA, the polynucleotide is made by nucleic acid synthesis while the antibody is raised by immunization. Furthermore, the polynucleotide can be used for hybridization screening, the butyrylcholinesterase variant can be used for therapy and the antibody can be used to immunopurify the antigen, for example. The examination of all groups would require different searches in the U.S. Patent shoes and the scientific literature and would require the consideration of different patentability issues. Thus, the inventions I-IV are patentably distinct.

The methods of Inventions V-VIII differ in the method objectives, method steps and parameters and in the reagents used. The Invention of Group V recites a method of converting a camptothecin derivative to a topoisomerase inhibitor comprising contacting said camptothecin derivative with a butyrylcholinesterase variant comprising or functional fragment thereof; Group VI recites a method of treating cancer comprising

administering to an individual an effective amount of a butyrylcholinesterase variant comprising or functional fragment thereof; Group VII recites a method of converting a camptothecin derivative to a topoisomerase inhibitor comprising contacting said camptothecin derivative with a butyrylcholinesterase variant comprising or functional fragment thereof and an antibody that specifically binds EGFR and Group VIII recites a method of converting a camptothecin derivative to a topoisomerase inhibitor comprising contacting said camptothecin derivative with a butyrylcholinesterase variant comprising or functional fragment thereof and an antibody that specifically binds CD20.

The inventions of Groups VII and VIII are directed to methods that recite structurally and functionally distinct elements and are not required one for the other. The invention of Group VII requires an anti-EGFR antibody, which is not required by any of the other groups. Similarly, the invention of Group VIII requires an anti-CD20 antibody, which is not required by any of the other groups. The examination of all groups would require different searches in the U.S. Patent shoes and the scientific literature and would require the consideration of different patentability issues. Thus, Inventions of Groups V-VIII are separate and distinct in having different method objectives, method steps, parameters and reagents used and different endpoints and are patentably distinct.

Inventions I and V are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the butyrylcholinesterase variant of Group I can be used in a materially different method such as to raise antibodies in addition to the materially different method of Group V.

Inventions II and VII are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the antibody of

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Group II can be used in a materially different method such as to immunoprecipitate the antigen in addition to the materially different therapeutic method of Group VII.

Inventions III and VIII are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the antibody of Group III can be used in a materially different method such as to immunoprecipitate the antigen in addition to the materially different therapeutic method of Group VIII.

6. Restriction for examination purposes as indicated is proper because all these inventions listed in this action are independent or distinct for the reasons given above and there would be a serious search and examination burden if restriction were not required because one or more of the following reasons apply:

- (a) the inventions have acquired a separate status in the art in view of their different classification;
- (b) the inventions have acquired a separate status in the art due to their recognized divergent subject matter;
- (c) the inventions require a different field of search (for example, searching different classes/subclasses or electronic resources, or employing different search queries);
- (d) the prior art applicable to one invention would not likely be applicable to another invention;
- (e) the inventions are likely to raise different non-prior art issues under 35 U.S.C. 101 and/or 35 U.S.C. 112, first paragraph.

**Applicant is advised that the reply to this requirement to be complete must include (i) an election of a invention to be examined even though the requirement may be traversed (37 CFR 1.143) and (ii) identification of the claims encompassing the elected invention.**

The election of an invention may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election

shall be treated as an election without traverse. Traversal must be presented at the time of election in order to be considered timely. Failure to timely traverse the requirement will result in the loss of right to petition under 37 CFR 1.144. If claims are added after the election, applicant must indicate which of these claims are readable on the elected invention.

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Should applicant traverse on the ground that the inventions are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

7. The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. Process claims that depend from or otherwise include all the limitations of the patentable product will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is

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found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai*, *In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. Failure to do so may result in a loss of the right to rejoinder.

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

8. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Blanchard whose telephone number is (571) 272-0827. The examiner can normally be reached at Monday through Friday from 8:00 AM to 6:00 PM, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached at (571) 272-0832.

The official fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status

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information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/David J. Blanchard/  
Primary Examiner, A.U. 1643